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THE DETERMINATION OF ACETANILID AND PHENACETIN IN PHARMACEUTICAL PREPARATIONS.

By Joseph L. Turner and Charles E. Vanderkleed.

Although pharmaceutical literature abounds in methods for the qualitative detection of acetanilid and phenacetin and for distinguishing one from the other, a search has failed to reveal any methods for their quantitative determination save the one given by Puckner (Proceedings of A. Ph. A., Vol. 53 [1905], p. 289), which, however, can be successfully applied only to mixtures containing, besides acetanilid, inorganic salts and alkaloids. This method at once becomes unreliable whenever the composition of the mixture is rendered more complex by the presence of other organic constituents.

The necessity, therefore, for a method which will permit of the estimation of acetanilid, or phenacetin, in a mixture, no matter how complicated it may be, is self-evident, especially in view of that provision of the Food and Drugs Act of June 30, 1906, which requires an accurate statement on the label of the amount of acetanilid or phenacetin present in a preparation.

For the estimation of acetanilid, taken as such, two methods are possible:—

I. Saponification of the acetanilid by means of an alkali; distillation of the resulting anilin from an alkaline solution; acidulation of the distillate with hydrochloric acid; diazotization by means of sodium nitrite at low temperature; and finally, combination with beta-naphtol-alpha-disulphonic acid.[1] The amount of azo-dye thus formed can be estimated by colorimetric comparison with a solution

[1] Reverdin and Harpe, *Berichte*, 22, 1004.

of the same dye prepared from a known quantity of freshly distilled anilin.[1]

II. Saponification of the acetanilid by means of an alkali; distillation of acetic acid from the resulting acetate, from an acid solution; and titration of the distillate.

It can readily be seen that Method I. is too elaborate for practical purposes, and the necessity for using a colorimetric method at the end renders it unreliable to a certain degree. Moreover, the difficulty of the operation of diazotizing, for which too much skill cannot be acquired, renders the method unavailable to the ordinary analyst. There remains, therefore, only Method II. for convenient use in an analytical laboratory.

The method for estimating acetic acid in acetates by means of distillation of the solution acidified with phosphoric acid was originally recommended by Fresenius.[2] Some years later Erdmann and Schultz,[3] followed soon after by Buchka and Erk,[4] and by Schall,[5] applied this method, though in form of a less successful modification (acidulation with sulphuric acid), to the estimation of acetic acid split off from acetylized products by means of saponification. Herzig,[6] shortly after the publication of Erdmann and Schultz's work, made use of phosphoric acid in this process, which thus received erroneously the name of "Herzig's Method."[7]

As applied by the authors to acetanilid, the method can be worked as follows:—

One gramme of acetanilid is saponified by heating to boiling, under a reflex condenser, for one and a half to two hours with 3 grammes sodium hydroxide, 20 c.c. alcohol, and 10 c.c. water. The solution is then transferred to an evaporating dish and the alcohol is evaporated off on the water-bath. The residue is transferred to a separator and shaken out once with ether in order to remove the anilin split off from the acetanilid. The ethereal solution is shaken

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[1] Bucherer and Schwalbe, *Berichte*, 39, 2798.

[2] *Zeitschrift für Analytische Chemie*, 5 (1866), 315.

[3] Liebig's *Annalen der Chemie und Pharmacie*, 216 (1882), 232.

[4] *Berichte*, 18 (1885), 1139.

[5] *Berichte*, 22 (1889), 1561.

[6] *Monatshefte für Chemie*, 5 (1884), 90.

[7] H. A. Michael, *Berichte*, 27 (1894), 2687. Ciamician, *Berichte*, 28 (1895), 1395.

out twice with water in order to recover traces of sodium acetate, which is somewhat soluble in ether, and the washings united with the original aqueous residue.

The water solution is then transferred to a flask of 1 litre capacity, acidified with about 25 c.c. of 85 per cent. phosphoric acid, and the acetic acid is distilled off with steam. (It is advisable to connect the flask with the condenser by means of a Kjeldahl's connecting bulb tube, so as to prevent the carrying over of phosphoric acid into the distillate.) The distillation is interrupted when the distillate no longer reacts acid to litmus. Usually about two hours are required, and from 800 to 1000 c.c. of distillate will have been collected before this point is reached.

The distillate is then titrated against sodium hydroxide, using phenolphtalein as indicator. We have found it best to titrate against N/1 sodium hydroxide with the addition of 1 c.c. of 1 per cent. solution of phenolphtalein. In spite of the large amount of liquid, the end-reaction is distinctive under these conditions to within 0·025 c.c. of N/1 sodium hydroxide.

One cubic centimeter of N/1 sodium hydroxide is equivalent to 0·13409 gramme acetanilid.

The following results were obtained, working on pure acetanilid:—

I. Acetanilid taken, 1·00 gramme; amount found, 0·9953 gramme.
II. Acetanilid taken, 1·00 gramme; amount found, 0·9972 gramme.

In order to determine the general applicability of this method to miscellaneous pharmaceutical preparations, the three following mixtures were analyzed for acetanilid:

I.—AN ELIXIR CONTAINING IN ADDITION TO 35 PER CENT. OF ALCOHOL AND 0·947 GRAMME OF ACETANILID IN 100 C.C., THE FOLLOWING INGREDIENTS:—

Extract of Indian Cannabis,
Caffeine,
Sodium Bicarbonate,
Sodium Salicylate,
Monobromated Camphor,
Extract of Hyoscyamus,
Fluid Extract of Gelsemium,
Fluid Extract of Celery Seed,
Aromatic Spirits of Ammonia.

In order to prepare the acetanilid content of this mixture for the saponification, the following procedure was adopted:

Of the elixir 150 c.c. were evaporated on the water-bath at a low temperature to remove all alcohol. The residue was shaken out four times with chloroform and the completeness of the extraction of acetanilid was checked by means of the iso-nitrile test. The united chloroform solutions were evaporated to a small volume in an Erlenmeyer flask on the water-bath, taking care that no active ebullition occurred during the process of concentration. The last portions of chloroform were driven off by means of repeated addition and distillation of small portions of ether. (The complete removal of chloroform is necessary in order to avoid the production of the disagreeable odor of phenyl isocyanide during the next step of saponification.) The resulting impure acetanilid was then saponified and the product of the reaction treated further, as per the process given above.

The results obtained were as follows:

I. Acetanilid present, 1·4205 gramme; amount found, 1·470 gramme.
II. Acetanilid present, 1·4205 gramme; amount found, 1·425 gramme.

II.—A MIXTURE OF ACETANILID AND SALOL.

This is a mixture very much used in medicine, and the determination of acetanilid in it is of special interest in that it so well shows the general practicability of the method proposed by us. The difficulty which here presents itself lies in the fact that while saponifying the acetanilid, the salol is also saponified, and when the mixture is acidified with phosphoric acid and distilled, phenol comes over together with acid, and may interfere with the titration. We therefore used the following modification of the method outlined above:

After the saponified mixture was acidulated with phosphoric acid, it was shaken out once with ether. All phenol was thus removed, but in order to avoid loss of acetic acid, the ethereal solution was shaken out three times with water, and the washings united with the original acid solution. The distillation with steam was then conducted in the usual way, and the distillate titrated.

The following results were obtained:

I. Amount taken, acetanilid 1·0 gramme and salol 1·0 gramme; acetanilid found, 1·003 grammes.

II. Amount taken, acetanilid 1·0 gramme and salol 1·0 gramme; acetanilid found, 0·9985 gramme.

III.—A MOIST ANTISEPTIC GAUZE, CONTAINING ACETANILID, ZINC SULPHO-CARBOLATE, POWDERED ALUM, BORIC ACID, THYMOL, MENTHOL, EUCALYPTOL, AND FORMALDEHYDE.

The gauze had been prepared by saturating the cloth with a hot aqueous solution of the above ingredients, and as it was an impossibility for the cloth to take up all of the solution, the reliability of the results obtained on analyzing the preparation can be judged only by the closely concordant figures obtained by the two slightly different methods pursued.

One yard of the gauze was divided into two parts. The first part, which weighed 51·35 grammes, was exhausted completely in a Soxhlet apparatus with chloroform, and the chloroform solution was treated as in the method for the analysis of the elixir given above. The second part, which weighed 48·5 grammes, was extracted in a Soxhlet apparatus with alcohol, as it was supposed that the chloroform might not have been able to penetrate the moist gauze sufficiently well to extract all of the acetanilid. The alcohol solution was then carefully evaporated, the residue was taken up with water and the aqueous solution was shaken out with chloroform, after which the usual method of procedure was pursued.

The results obtained were as follows:

I. Weight of gauze taken, 51·35 grammes; acetanilid found, 0·93863 gramme = 1·828 per cent.

II. Weight of gauze taken, 48·5 grammes; acetanilid found, 0·89840 gramme = 1·852 per cent.

Conclusion.—The method can be applied to the most complicated pharmaceutical mixtures, it being necessary, in general, only to extract the mixture with chloroform or alcohol in order to obtain the acetanilid in a state of sufficient purity for the saponification. If, after saponification, and on acidulation with phosphoric acid, volatile acids other than acetic acid obtained from the acetanilid are present, means must be taken to remove them before carrying out the distillation, as for example, the removal of phenol by means of ether.

As phenacetin is closely related, chemically, to acetanilid, all that has been said with regard to the latter applies equally well to the

former. For that reason we did not deem it necessary to verify the general applicability of our method to preparations containing phenacetin. (One cubic centimeter of N / 1 sodium hydroxide is equivalent to 0·17779 gramme phenacetin.)

The simultaneous presence of acetanilid and phenacetin, as well as other acetylized compounds, in the same preparation would, of course, prevent the use of this method. The authors, however, are engaged in working out a method for the quantitative separation of acetanilid or phenacetin from other acetylized compounds in pharmaceutical preparations, the results of which will be contributed in a later communication.

Other interferences which should be mentioned are acetates, nitrates, and nitrites. These salts, if present in the mixture to be analyzed, would be left behind by means of the chloroform extraction, but their presence in the phosphoric acid or in the alkali used for saponification must be guarded against. The presence of chlorides does not interfere with the results of analysis, as the phosphoric acid cannot liberate the hydrochloric acid from its salts, and in this particular lies the advantage of phosphoric acid over the sulphuric acid used by Erdmann and Schultz.

Finally, if carbonate be present in the alkali used for saponification, the carbon dioxide formed on addition of phosphoric acid must be guarded against, as it would be distilled over with the acetic acid and vitiate the result of the titration. To this end, it is advisable to heat the acidified solution to boiling for a short time, under a well-cooled reflux condenser, before the distillation with steam, in order to drive off the carbonic acid gas.

All stoppers and connections must be of rubber, as cork absorbs acetic acid.

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SOME NOTES ON OPIUM FROM THE COMMERCIAL STANDPOINT.

BY C. M. KLINE.

For the benefit of those not very familiar with opium the writer offers this preliminary paragraph. Opium is produced by many

countries in the East and differs largely in its appearance, odor and strength according to the country or district in which it is produced, both on account of natural causes and differences in the methods of handling. The names applied to opium in this way are almost innumerable and many appearing on brokers' lists have become so garbled as to be scarcely recognizable. In practically all cases, however, they may be traced to the villages or towns from which that particular variety hails, and by consulting the map all may be gathered under one or another of the main geographical groups. When once so gathered they are often again arranged according to their quality as determined by their appearance and assay. Under the main divisions we have Turkey opium, including the opium of Asia Minor and European Turkey, Persian opium, East India opium, Egyptian opium, and Chinese opium. Occasionally we hear of opiums produced in small quantities in other countries that have little or no commercial importance; Bulgarian, Zambesi or Mozambique are types of such opiums. As Turkey opium is of the greatest importance in the United States we will consider this first.

TURKEY OPIUM.

The opium produced in Turkey is the most important commercially, and is beyond all comparison the most widely known in the markets of the world. This opium is the kind generally understood as meant when opium for use in medicine is mentioned, and any other kind should be used only after careful consideration. In fact many pharmacopœias recognize only that opium collected in Asia Minor. Turkey opium is marketed through three important ports, Smyrna, Constantinople, and Salonica. Of these three great markets, Smyrna is most important and is said to handle five-eighths of the total output, and to fix the price for all the markets of Turkey. The principal commercial varieties are as follows:—

Boghaditz, derived from the district of that name, lying north of Smyrna, between that place and Constantinople. It is the richest opium obtainable in Asia Minor, so far as the morphine content is concerned. It is expensive and seldom shipped to America. It is very gummy and on that account the morphine is difficult to extract in assaying.

Yerli. This name when translated means "surrounding" and is used to indicate all that opium from the districts surrounding

Smyrna, except Boghaditz. It produces an opium rich in morphine, but not sightly. It is very soft and poor in appearance. It is the quality most in demand for the manufacture of morphine.

Karahissar. This grade is derived from the territory lying next beyond the district known as Yerli and further away from Smyrna. It covers practically all the interior of Asia Minor with the town of Karahissar as its centre. The opium is generally sightly, some more so, some less. The poorer grades are shipped as jobbing opium (Adet). The better grades are particularly sightly and are shipped only on special orders, as they cost somewhat more. The higher grades from that district are also known as "Selected Karahissar," and run as a rule as high in test as the Yerli opium and are mostly bought for mixing with the Yerli for manufacturing purposes. The morphine content is said to average about 11·5 to 12 per cent.

Adet. This word as used means "common." It is the opium sometimes called "Jobbing Opium" and originally described the opium of inferior grades from all districts. The quality of this grade, however, has become so poor that in modern practice it is often necessary to mix it with a better quality opium before it can be placed upon the market.

Salonica opium includes all opium produced in European Turkey, and marketed through the port of Salonica. Formerly it was of very fine quality, some assaying as high as 14 per cent., and not much of it was produced. Of later years it has grown in importance, until now Salonica markets about one-third of the total opium in Turkey. The quality is somewhat poor, some shipments are said to test as low as 10 per cent. The finer, softer grades are often shipped to this country and, without being assayed, are inspected while in bond by merchants of Cuba and the South American ports, who select from the cases those lumps of the best appearance and re-ship them to their native lands to be used in smoking. For this opium they are willing to pay a high price. The residues are then utilized in the regular channels.

Tokat and Malatia opiums are produced in the districts by that name located in Armenia on the southeast side of the Black Sea. Of the two, Tokat is the most plentiful and the best known. They are sold in the Constantinople markets for export to Cuba, West Indies, Central and South America. They are largely of a light

color, fine, smooth texture and used for the most part for smoking. The morphine content is stated to vary from 7 per cent. all the way to 14 per cent. This opium sells from 2 shillings to 3 shillings 6 pence per pound higher than Smyrna opium and is largely known as "selected shipping opium for smoking purposes."

Turkey opium is generally marketed in the form of rounded masses, which according to their softness become more or less flattened or many sided or irregular, by mutual pressure in the cases in which they are packed. The lumps vary greatly in weight, but the majority are between one-half to two pounds. The exterior is covered with the remains of poppy leaves strewn over with rumex chaff and fruit. This is done to prevent the lumps from adhering, and, as far as we know, is practised only on Turkey opium. The interior is coarsely granular, varying in color from light chestnut to blakish brown. In general it may be said that light-colored, soft, gummy opium is fine quality and will assay high in morphine, while hard, dark opium, unless this condition is the result of years of keeping, will assay low in morphine.

A term which is very frequently read in connection with opium is "Talle-Qualle," in some such way as "Superior Talle-Qualle Opium." This term means, "as it runs," the understanding being that the purchaser is obliged to take the opium as tendered by the seller with the exception only that he may discard that which is not natural opium at the examination. Another term is "Visited Opium." This expression means that any part of the opium not up to the full test may be rejected.

When an opium that is quite fresh is purchased in the markets of Turkey, it is customary for the brokers to demand an allowance for the amount of moisture in the opium, and they in turn expose the balls until such time as the opium has attained the necessary firmness, when it is ready for shipment. The charge for drying opium in Smyrna is 2 pence per pound and the loss in weight is approximately 23 per cent.

PERSIAN OPIUM.

Persian opium occasionally appears in the United States, largely for use in manufacturing, though it is also prized for smoking purposes. When the crop is small and the price is high, Persian opium finds its way only to the Chinese markets. If, however, the crop is

large and the price, therefore, somewhat more reasonable, some Persian opium finds its way into the London markets and through this channel often to America. It is usually found in hard blocks, brittle and free from leaves without any rumex chaff. Each separate block is wrapped in paper, generally red, though sometimes yellow. It is very high in morphine, smooth, running from 12 to 14 per cent.

EGYPTIAN OPIUM.

Egyptian opium is only produced in small quantity, though occasionally a few cases appear in the London markets. It is very low in morphine content, assaying only from 6 to 7 per cent., and is of a dark color.

INDIA OPIUM.

India opium is marketed almost entirely in China and is never seen in Western markets. It also contains a very small amount of morphine and is said to assay only about 7 per cent.

The United States Customs demand that opium to enter the country shall assay 9 per cent. or over. The various grades differ so largely in their texture and their content of gummy matter that it is often difficult to obtain anything like accurate results in assaying, particularly when a sample is submitted which is of a different quality than that customarily handled by the individual engaged in the assay. Often much trouble has been caused the broker through the fact that the individual peculiarities of the various analysts figure so largely in the results obtained. One house of which we have heard, because of some new improvements in their assaying process, obtain results regularly 2 per cent. lower than the Government assay made in Smyrna and guaranteed under that strength.

CONTRIBUTION FROM THE RESEARCH LABORATORIES
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SOME WELL KNOWN SYNTHETIC CHEMICALS AND THEIR RELATION TO THE PURE FOOD AND DRUGS ACT.[1]

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The word "synthetic," as used in the chemical world, means a combination of separate substances, elements, or radicals, which

[1] Delivered before the Franklin Institute, Philadelphia, January 10, 1907.

result in the formation of definite chemicals. The manufacture of acetanilide from benzol, or antipyrine from aniline, affords good illustrations, inasmuch as in the manufacture of both several operations are necessary. The word "synthetic," however, has acquired an entirely different meaning which has been used to a considerable extent in the past, usually in an honorable manner, but often for the purpose of deceiving not only the public, but also the doctor as well. This feature has been claiming recognition in no unmistakable terms during the past few months. It is held by some that the mixing together of the various cinchona alkaloidal salts, in proportion as found by analysis of the cinchona barks, the same dissolved in simple elixir and colored with caramel, is a "synthetic elixir of cinchona bark." Other illustrations are the common headache mixtures, which consisted in the past, and at present to a lesser extent, chiefly of acetanilide, sodium bicarbonate, or ammonium carbonate, and caffeine. These mixtures are at times so named as to lead to the belief that they are synthetic chemicals. In some cases even a hypothetical chemical name, together with a structural formula, are attached to make the deception even more complete. Since the passage of the act, the acetanilide has been replaced in many instances by para acetphenetidin (commonly known as phenacetine) and antipyrine. This subject will be considered in a subsequent portion of this paper. It is also claimed that a so-called "raspberry extract" made up with various esters dissolved in alcohol (grain or wood) and colored with cudbear is a "synthetic raspberry extract." There are undoubtedly different views as to whether or not the latter claims are justifiable, but in the speaker's opinion, the first definition, or a similar one, is the only one that should receive any recognition in the chemical world. As a matter of fact, the latter is simply used to attract the attention of the public and has no basis for existence whatever.

The Pure Food and Drugs Act specifies that an article is misbranded if it fails to bear a statement on the label of the package "of the quantity or proportion of any alcohol, morphine, opium, cocaine, heroin, alpha or beta eucaine, chloroform, cannabis indica, chloral hydrate, or acetanilide, or any derivative or preparation of any such substances contained therein." The act also forbids the use of any poisonous or deleterious ingredient in the manufacture of food products, or any agent which misleads or deceives in any par-

ticular. The two phases of the act just considered require, first, that the presence of certain habit-forming drugs shall be declared on the label, and second, no injurious agent or agents which deceive in any particular shall be used in the manufacture of food products.

It can readily be seen by chemists familiar with the ingredients enumerated in the act that the phrase "derivative and preparation of same" is very comprehensive, which was undoubtedly the intention of Congress. This clause was undoubtedly introduced for the purpose of preventing or evading prosecutions under the law on pure technicalities. For example, it has been held by the defendant in a number of cases where a prosecution was brought, on the ground that a product contained the forbidden ingredient, morphine, that the ingredient present in the product under consideration was not morphine, but morphine sulphate. The same position has been taken in other cases; for example, it is contended by some manufacturers that the introduction of cocaine through the medium of an extract of coca leaves, or by extracting coca leaves directly with the menstruum of the article, cannot be considered a cocaine preparation any more than could coffee be construed as a caffeine product. It is immaterial how cocaine is introduced into a product; the fact of its presence renders such a product a cocaine preparation. Any other conclusion must be based on a technicality or is a mere quibble.

So far as the word "preparation" is concerned, as used in the act, there does not appear to be any question relative to its meaning, but this is not the case with the word "derivative." The term "derived from," as used in the tariff law of 1897, has not only been subject to decisions at the hands of the Appraiser of the United States Customs Service, but has also been defined by the United States Federal Court (1899 Federal Reporter, 719) and the United States Court of Appeals (1902 Federal Reporter, 603). The decisions arrived at are that the words "derive," "derivation," "derivative," must be interpreted as "made of," "prepared from," "produced from," "obtained from," and that the term "derived from" has its ordinary meaning of "produced from" and relates to the physical substance from which such product is obtained and ***not to its chemical relationship.*** In other words, if the manufacturer starts with alizarine and by partial replacement produces a dye, such

dye is derived from alizarine, but not otherwise. The question under consideration in the above decisions was whether or not certain dyes were derived from alizarine. These precedents must undoubtedly be taken into consideration in connection with the recently enacted pure food and drug law, but the aims and objects of the latter are entirely different from those of the tariff law.

The meaning of the term "derivative," as used in the act, has been called into question because (para) acetphenetidin is classed as a derivative of acetanilide. There is no question but that (para) acetphenetidine is a derivative of acetanilide, both chemically and physiologically, and resembles it in its tendency to habit formation, physiological action, and physical properties. Furthermore, Treasury decision 13,270 construes this chemical as an alcoholic medicinal preparation. The exact status of this product under the law therefore appears to be in a somewhat unsettled condition at present.

In this paper only a few of the synthetic chemicals that are affected by the Federal law will be considered. For the purpose of ready reference, it is deemed desirable to collect them into the following groups:

(1) ALCOHOL GROUP.

Common Names.	Synonyms and Chemical Names.
Ether	Sulphuric ether, ethyl ether.
Ethyl acetate	Acetic ether.
Ethyl nitrite	
Ethyl bromide	Monobromethane.

(2) CHLOROFORM AND CHLORAL HYDRATE GROUP.

Chloroform	Trichlormethane.
Chloral hydrate	Trichlorethidene glycol.
Chlorotone	Aneson; Acetone chloroform; Trichlorpseudobutyl-alcohol.
Chloral alcoholate	Trichlorethidene ethyl alcoholate.

(3) COCAINE GROUP.

Alpha Eucaine	Benzoyl-Methyl-tetra-Methyl-gamma-oxy-piperidin-carboxylic-Methyl ester.
Beta Eucaine	Benzoyl-vinyl-diacetonalkamin hydrochloride.

(4) OPIUM-MORPHINE GROUP.

Heroin	Diacetyl morphine.
Dionine	Ethyl morphine hydrochloride.
Peronine	Benzylmorphine hydrochloride.
Codeine	Methyl morphine.

(5) ACETANILIDE GROUP.

Acetanilide	Phenylacetamide; Antifebrine.
Phenacetine	Para-acet-phenetidin; Acetphenetidin; Para-acet-amido-phenetol; Para-oxyethyl-acetanilide.
Antipyrine	Analgesin; Anodynine; Parodyn; Phenazon; Phenyl-dimethyl-pyrazolon; Pyrazine.

(6) PRESERVATIVE, SWEETENING AND FLAVORING GROUP.

Salicylic acid	Ortho-oxy-benzoic acid.
Benzoic acid	
Vanillin	Methyl-protocatechuic aldehyde.
Saccharin	Benzosulphinide.

In the above groups it will be noticed that not only are the common names employed, but also the synonyms and structural formula names. The object of giving the latter is simply to call attention to the fact that manufacturers are making frequent requests to be permitted to use some other words than those specifically enumerated in the act; for example, one manufacturer represents that a setting forth on a label of the fact that his product contains opium would be a financial loss and asks whether it would not be satisfactory to state on the label that this product contains a certain amount of Papaver somniferum. Other manufacturers request that they be permitted to use the word phenylacetamide, or the phrase "the monacetyl derivative of aniline," or the structural formula in place of the word acetanilide. If it were permitted to use other words than those given in the act for the ingredients specifically covered, there would soon be such a confusion of names and structural formulæ that it would be necessary to consult an expert organic chemist to decipher same.

It is held by some writers that it was absolutely unwarranted to include some of the chemicals and products enumerated in the rules and regulations, because in many cases such articles are never used as habit-producing drugs. In this connection it should be stated that this question was submitted to about twelve of the best pharmaceutical chemists, manufacturing and analytical, and while a few think that the public would be protected just as well without requiring a declaration on the label of the presence of certain ones, yet on the whole every one heard from thus far suggested additional products to be included. In other words the suggestions of these men indicate that instead of having included too many drugs, the list should be augmented. Our general correspondence confirms this

attitude. It should furthermore be noted that it seems necessary to include certain chemicals in order to avoid technicalities; for example, it is held by one chemist that a certain chemical could not be considered a derivative of alcohol because ethyl bromide is not enumerated as a derivative of alcohol in the regulations, and inasmuch as this chemical is employed directly in introducing the ethyl group into the product, it is necessary that this product be included as a derivative of alcohol. The contention that certain ingredients are not used as habit-producing drugs is not well taken. This claim is made for ether, which, as a matter of fact, however, is used to fortify beverages in order to render intoxication more rapid and complete; particularly is this the case where parties are addicted to the alcohol habit and the ordinary beverage does not appear to satisfy the appetite of the consumer.

The morphine group presents some interesting features. It is well known that morphine and opium, and the disastrous results of same, have been widely exploited during the past few years, not only in the lay journals but also to some extent in the public press. Many manufacturers deem it expedient to remove these words from their labels if possible because of this unfavorable notoriety. The result is that these ingredients have, in many instances, been replaced with other products which are not so well known to the public; for example, heroin, codeine and dionine have replaced morphine in a considerable number of cases. These chemicals are at present supposed not to produce as deleterious results on the human system as do opium and morphine even when used over extended periods, but what the future will bring forth by their promiscuous and indiscriminate use, is difficult at present even to conjecture. It is even now reported that where narcotic laws prohibit the indiscriminate sale of morphine and no restrictions whatever are placed upon the sale of codeine, that the latter product is being used in place of the former.

What has been said above in connection with the opium-morphine group applies equally to the acetanilide group. At the time the Pure Food and Drugs Act was passed there were approximately 500 headache and laxative preparations sold through the jobbing trade under various names which contained acetanilide. It is a significant fact that the acetanilide in many of these preparations has been replaced by acetphenetidin (phenacetine), and we are also informed,

from various sections of the country, that antipyrine is being employed for the same purpose. Exactly why some of these changes have been made is not clearly apparent, because none of the substitutes are as cheap as acetanilide; although the price of each has been materially reduced within the past few years. This is due largely to the fact that the patents covering these chemicals have lapsed, and the price has fallen in the case of acetphenetidin (phenacetine) from $16 to $1 per pound, and antipyrine from about $22 to $2.40 per pound, both in bulk. The price of acetanilide in quantity at this writing is 25 cents per pound. Another probable reason for replacing acetanilide by acetphenetidin is because the latter is supposed to have a less deleterious effect upon the human system than the former, but this is at present an open question. No one has thus far ventured to give this as an excuse for using antipyrine, because it is a well known fact that the latter is the most dangerous of these three medicinal agents. Two other potent factors, however, should be considered in this connection. These are: (first), that the deleterious effects of neither acetphenetidin nor antipyrine have been given any publicity, and the public therefore has little knowledge of the meaning of the words acetphenetidin and antipyrine, should their presence be declared upon the label; (second), it was expected that both of these chemicals could be used indiscriminately in medicines without the necessity of declaring their presence upon the label. Acetphenetidin, however, according to the rules and regulations made under the Pure Food and Drugs Act, must be set forth on the label.

The use of harmful preservatives in food products is forbidden. The exact status of the harmful nature of certain preservatives is at present not definitely settled. Among the most conspicuous preservatives used during recent years are the synthetic chemicals known as salicylic acid and benzoic acid and their salts. The experimental results obtained in the Bureau of Chemistry in connection with salicylic acid and the salicylates have just been published in Bulletin 34, Part 2, from which part of the general conclusions are herewith quoted:

"There has been a general consensus of opinion among scientific men, including the medical profession, that salicylic acid and its compounds are very harmful, and the prejudice against this particular form of preservative is perhaps greater than against any other

material used for preserving foods. This is due not only to the belief in the injurious character of salicylic acid, but perhaps is especially due to the fact that it has in the past been so generally used as an antiseptic. That salicylic acid should be singled out especially for condemnation among preservatives does not seem to be justified by the data which are presented and discussed in this bulletin. That it is a harmful substance, however, seems to be well established by the data taken as a whole, but it appears to be a harmful substance of less virulence than has been generally supposed. The addition of salicylic acid and salicylates to foods is therefore a process which is reprehensible in every respect, and leads to injury to the consumer, which, though in many cases not easily measured, must finally be productive of great harm."

Benzoic acid and the benzoates are by many considered less harmful than the salicylates. Whether or not this is correct remains to be established by future experiments and observations. This much, however, is certain, that whenever it is possible, and usually it is, food products should be prepared without the use of any questionable preservative.

Saccharin is generally employed as a sweetening agent and its use is largely of a deceptive character because the consumer usually believes that when he is eating a food product sweetened with this chemical, that the sweetening is due to some form of sugar. The use of saccharin as a sweetening agent is not only common in food products, but also in medical remedies. Saccharin is a most valuable agent for certain diseased conditions, but this does not justify its indiscriminate use. Inasmuch as deceptions and misrepresentations of all kinds are prohibited under the act, the presence of this chemical should be declared upon the label.

The synthetic production of vanillin undoubtedly was one of the greatest scientific achievements and triumphs of chemistry. Vanillin is a very valuable commodity. It is claimed by many that flavoring preparations made with vanillin as a basis, possess distinct advantages over extracts from the vanilla bean. There is no question whatever but that vanillin possesses certain merits not inherent in the vanilla bean, and it seems rather incomprehensible why manufac turers do not take advantage of this fact and sell vanillin preparations on their merits. Let not vanillin in disguise deprive extract of vanilla of its time-honored reputation.

THE CHEMISTRY OF THE PROTEINS AND THEIR RELATION TO BIOLOGY.[1]

By Emil Fischer.

It is not surprising that substances of such eminent importance as the foodstuffs have long been the subjects of scientific investigation, when it is remembered that the great majority of the people pay out more than one-half of their incomes in purchasing them. Physiology, chemistry, botany, and medicine strive to establish their value, their composition, their formation in the plant world, and their fate in the animal kingdom. Generally speaking, foodstuffs show great similarity in chemical composition, though differing widely in outward form, in color, taste, and smell; for the great majority consist of complicated compounds of carbon, or so-called organic substances, built up by remarkable synthetic processes in plants from very simple materials—namely, water, carbon dioxide, nitrates, and a few other salts found in the earth. These products then undergo manifold changes in the animal body—sometimes a radical decomposition previous to being used for the building up of the organs, and, finally, they are reconverted into the materials from which they were made—namely, carbon dioxide, water, etc. For the correct interpretation of these changes it is necessary to acquire an accurate knowledge of the chemical nature of each individual substance, which occurs at any time during the cycle, and this is the problem which, for the last one hundred years, organic chemistry has tried to solve—always with increasing success.

THREE GROUPS OF FOODSTUFFS.

The large number of organic compounds which have in this way to be considered may be fairly sharply divided into three classes—the fats, the carbohydrates, and the proteins, as, apart from water, they form the major portion of our nutriment. Their composition was proved, qualitatively, in the eighteenth century by Lavoisier, and, quantitatively, with fair accuracy, in the beginning of the nineteenth century. But of much more importance and of greater difficulty to ascertain is their constitution, or the structure of their molecules, and in this respect our knowledge of the three classes

[1] Abstract of a lecture delivered before the Royal Prussian Academy of Sciences; reprinted from *Pharm. Jour.*, March 2, 1907, p. 261.

differs widely. The nature of fats was essentially proved by the researches of Chevreul on the preparations of soaps in the first decade of the nineteenth century; and in 1854, or twenty-six years after the commencement of organic synthesis, Berthelot showed that it was possible to prepare the fats from glycerol and the fatty acids. Whereas it was not until 1890 that grape sugar—the most important member of the carbohydrate group—was artificially prepared, and the more complicated members—starch and cellulose—have not even now been synthesized, and, moreover, the size of their molecules is doubtful. Still more imperfect is our knowledge of the proteins (albuminoids), which differ from the fats and carbohydrates in containing nitrogen, and are, together with their numerous derivatives, the most complicated chemical substances which Nature produces. Typical of them is casein—obtainable in a variety of ways from milk and the white of egg—which is not, as generally supposed, an individual substance, but consists of at least two proteins resembling one another very closely. The property possessed by egg albumin of coagulating when heated is common to a large number of proteins. Blood is, however, richer in these substances than other animal secretions, containing four different classes, to which belong fibrin and globin. Two other proteins worthy of special mention on account of their simple chemical composition are (*a*) the protamines—of which the first representative was isolated by Miescher in 1874 from salmon spawn—and (*b*) fibroin, the principal constituent of silk, which, according to the author's experience, is the easiest of all proteins to study.

STRUCTURE OF THE PROTEINS.

As in the other chapters of organic chemistry, two methods are available for determining the structure of the molecules of the proteins—synthesis and analysis—and in connection with the latter, the only process which has given direct evidence is "hydrolysis," whereby there are first formed easily soluble products known as albumoses and peptones, which then further break down into amino acids. Such changes occur during digestion, and can be more rapidly brought about, artificially, by the action of strong acids, such as hydrochloric acid, which gives rise almost exclusively to amino acids. Among the more important of these may be mentioned glycocoll, alanine, valine, leucine, and isoleucine, which are

the *a*-amino derivatives of acetic acid and its homologues, containing three, five, and six carbon atoms; phenylalanine, closely related to analine, but containing the phenyl group; serine and tyrosine, the simple hydroxy derivatives of alanine and phenylalanine; aspartic and glutaminic acids; prolin and oxyprolin, derived from the heterocyclic compound pyrrolidine, and which form a sort of bridge between the proteins and the alkaloids; the diamino acids, ornithine, lysine, and arginine; histidine; tryptophan, belonging to the indol group; and cystin, characterized by its high content of sulphur.

It does not follow that all these acids must occur as degradation products of every protein, in which the molecule would be terribly complicated and have a value of 12,000–15,000, or from fifteen to twenty times that of the fats; but all are obtainable from the majority of the proteins, and, as they have been recognized for more than fifty years as the corner-stones of the protein molecule, it is not surprising to find that in most cases the structure is known and a complete synthesis has been effected. With the exception of glycocoll, all of them occurring in nature are optically active, whereas the synthetic products are inactive; but they can be split into optically active forms by the well-known methods of Pasteur.

This work only solves the smallest portion of the problem of the chemical constitution of the proteins, for it is much more difficult to answer the question in which way are the molecules of the amino acids bound together? It would appear that the solution should lie in the investigation of the products of partial hydrolysis of the proteins; but the resulting albumoses and peptones are mixtures of very similar substances, for which there are no known methods of separation. The author has therefore chosen the alternative method of investigation—namely, the synthesis of the proteins from amino acids—and has attempted to thereby produce artificial proteins similar to those occurring in nature.

SYNTHESIS OF "THE POLYPEPTIDES."

Starting with two molecules of glycocoll (glycine), it is seen that condensation can take place between the carboxyl group of one molecule and the amino group of the second molecule, giving rise to a new substance:—

$$NH_2\cdot CH_2\cdot CO\overline{|OH \quad H|}NH\cdot CH_2\cdot COOH =$$
$$H_2O + NH_2\cdot CH_2\cdot CO\cdot NH\cdot CH_2\cdot COOH \quad (1)$$

with which the process might be again repeated between the terminal amino group and the carboxyl group of yet another molecule of glycocoll, giving a body

$$NH_2\,CH_2{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}COOH \quad (2)$$

Such products receive the generic name "polypeptides"; when formed from two molecules of an amino acid they are dipeptides (glycylglycin, 1); from three molecules, tripeptides (diglycyl-glycin, 2), etc. The following may be quoted as illustrating the various methods employed for bringing about this type of reaction. Glycocoll is allowed to interact in aqueous alcoholic solution with the acid chloride of chloracetic acid:—

$$ClCH_2{\cdot}COCl + NH_2{\cdot}CH_2{\cdot}COOH = ClCH_2{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}COOH + HCl$$

and the chloroacetylglycin so formed is treated with aqueous ammonia, when the chlorine atom is replaced by an amino group giving glycylglycin (formula 1). The process then can be repeated to give tri-, tetra-, and pentapeptides; but it becomes tedious for the preparation of very complicated substances, which are obtained by a modification of the process. For example, pentaglycylglycin (3) is allowed to interact with the acid chloride of bromoisocapronyldiglycilglycin (4)

(3) $COOH{\cdot}CH_2{\cdot}NH(CO{\cdot}CH_2{\cdot}NH)_4{\cdot}CO{\cdot}CH_2{\cdot}NH\boxed{H}$

(4) $BrCH\,(C_4H_9){\cdot}CO\,(NH{\cdot}CH_2\,CO)_2{\cdot}NH{\cdot}CH_2{\cdot}\boxed{CO\,Cl}$

and the bromine atom in this body is then replaced by an amino group, giving leucyl-octaglycyl-glycin.

$$NH_2{\cdot}CH(C_4H_9){\cdot}CO(NH{\cdot}CH_2{\cdot}CO)_8NH{\cdot}CH_2{\cdot}COOH$$

About 100 of these polypetides have been prepared, mostly (on account of expense) derivatives of glycocoll, alanine, and leucine; but when cost and trouble have not to be considered it will be possible to prepare peptides from the most complicated of the amino acids.

IDENTITY OF POLYPEPTIDES WITH PROTEINS.

Some of the polypeptides have proved to be identical with certain degradation products of the peptones, and it is important to notice that they resemble closely in their properties the natural proteins.

For instance, a polypeptide containing the residues of fourteen amino acids (leucyl-triglycyl-leucyl-octaglycyl-glycin) when dissolved in alkalies froths like a solution of soap; it forms very insoluble salts with mineral acids and gives a beautiful biuret reaction. But it does not follow that these synthetic products need be identical with any natural proteins, for, though similar in the structure of their molecules, yet the kind, number, and arrangement of the amino acid residues may be quite different. It will only be possible to say that a natural protein has been synthesized when it has been definitely characterized as a chemical individual and proved to be identical with a synthetic product. This must be the trend of future work; peptones and albumoses must be separated and characterized, and still more complicated peptides built up from them. To attain this end means much laborious work, but the author has no doubt that success is possible. No commercial value is at present attached to the investigation as in the cases of organic syntheses, which have given to the world dye-stuffs, perfumes, synthetic remedies and explosives; the investigation of the proteins has at present the purely scientific aim of giving to biology a clearer insight into the chemical processes of animal and plant life.

THE PROTEINS AND ENZYMES.

The proteins are the material from which the organism builds up its most powerful agents, for as such the ferments or enzymes may be described without exaggeration. These can produce the most varied changes, such as oxidation, reduction, hydrolysis, and condensation, classical examples being found in the digestion of food in the stomach and intestines or in the preparation of alcoholic beverages from juices containing sugar by the action of yeast. The chemical investigation of the enzymes is still in its infancy; all attempts to decide their composition and structure have so far proved in vain; but it is known with certainty that they possess many resemblances to the proteins and are very probably formed from them. The fuller investigation of the proteins must therefore throw further light on the nature of the ferments, and the attempted synthesis of the latter from natural or synthetic proteins would not, even at the present time, be a rash enterprise. On account of the part which they play in the chemical processes of the living organism, ferments and proteins are so closely connected that their inves-

tigation must take place hand in hand. Progress will not be rapid, for even when the main methods of attack have been developed it will mean endless individual work; but this will be readily accomplished by science, through the co-operation of numerous voluntary workers and the help obtainable from modern institutions.

"Organic synthesis is not yet eighty years old, for it commenced in 1828, when Wöhler synthesized urea. Will it rule over the province of the natural proteins and ferments on its hundredth birthday? No definite answer can be given, but it is certain that the question will never disappear from the domain of organic chemistry, and its solution would be a powerful advance for general biology, for medicine, and for many economic problems."

A RETROSPECT OF DISCUSSIONS ON THE RENEWAL OF PRESCRIPTIONS.[1]

By John K. Thum, Ph.G.

The renewal of the prescription, like the ownership, has long been a source of much discussion among physicians as well as among pharmacists. Just forty years ago a number of papers, bearing on this subject, appeared in the medical and pharmaceutical journals of this country, and, among others, the East River Medical Association of New York even went so far as to propose legislation to regulate and control the renewal of all prescriptions.

At the sixteenth annual meeting of the American Pharmaceutical Association, held in Philadelphia in September, 1868, the members present discussed a communication from the East River Medical Association of New York, and appointed a committee of five members to draft suitable resolutions regarding the renewal of prescriptions.

In the course of the discussion leading up to the appointing of this committee, Dr. Squibb expressed the opinion that "this Association may pass any rule it pleases in regard to the matter, but it cannot bind common usage. A physician who gives a fluid ounce of syrup of rhubarb, and asks that that prescription shall never be repeated, prescribes to that pharmacist that he shall never sell any

[1] Abstract of paper read at the meeting of the Philadelphia Branch of the American Pharmaceutical Association, March 5, 1907.

more syrup of rhubarb to that person. If the syrup of rhubarb can never be again sold without a written prescription it obstructs the thing entirely. Any article in common use may be excluded from sale by such a regulation as that. I mention this as an extravagant case to show that no such rule as is proposed here ever could be adopted with justice." Dr. Squibb further asserted that it would be a hardship upon the physician to be obliged to write a prescription for every simple remedy, but that, on the other hand, the pharmacist should, and no doubt would, refuse to put up a prescription containing potent or habit-forming drugs, or one that was otherwise injurious in character. In concluding he said: "It is a thing that cannot be laid down by law. It must depend upon the education of the pharmacist, who must be educated to have such judgment as to be able to decide these minor points."

The committee appointed to consider the subject of the renewal of prescriptions subsequently presented a preamble and resolution asserting, among others, that:

"The Association regards the pharmacist as the proper custodian and the owner of the physician's prescription."

"The restriction of the pharmacist to a single dispensing of a prescription, without the written authority of the prescribing physician for its renewal, is neither practicable nor within the province of this Association."

"Nevertheless we regard the indiscriminate renewal of prescriptions, especially when intended for the use of others than those for whom they were prescribed, as neither just to the physician nor to the patient, between whom we stand as conservators of the interest of both, and that such abuses should be discouraged by all proper means."

It is quite evident that the matter of the renewal of prescriptions was considered by these pioneers of American pharmacy from a common-sense point of view. Dr. Squibb brought the question down to its only legitimate solution, that of education and proper training. If teachers in pharmaceutical schools would, at appropriate times, impress upon their students the necessity and value of a cultivation of the moral sense and instill in them a nice sense of honor, the renewal of prescriptions as well as other abuses which are lowering the tone of true pharmacy would correct themselves in short order.

The pharmacist can and should refuse to repeatedly renew a prescription containing potent or habit-forming drugs, and he should also refuse to renew prescriptions that are designed for the treatment of genito-urinary disorders or for the producing of abortion.

In doing so, however, the pharmacist should and must use tact, always remembering that his vocation in life should be to protect the patient, please the physician and make an honest living.

To me the most rational method for controlling the indiscriminate renewal of prescriptions is that described by Mr. Burke, of Detroit, at the Golden Jubilee meeting of the American Pharmaceutical Association in Philadelphia, in 1902. Mr. Burke attaches to all containers of medicines prescribed by physicians a sticker with the following notice:

"Much harm often results from refilling prescriptions. It is always best to obtain the advice of your physician."

The general use of a sticker like this on all prescriptions that should not be renewed without positive orders from the physician, would be a practical step in the right direction. A warning of this kind would make people solicitous for their welfare. They would probably consult their physician and be guided accordingly.

The argument that is sometimes advanced that the physician is not receiving adequate compensation when his prescriptions are renewed without his order is a wrong one, and is repudiated by all physicians of standing. The question obviously should not be allowed to resolve itself into what is best for the physician or the pharmacist, but, rather, what is good for the public at large? The public have rights which we must take into account. Any method that will contribute the greatest good to the greatest number is always the one to be sought for.

AN EFFICIENT PLAN FOR CONTROLLING THE RENEWAL OF PRESCRIPTIONS.[1]

By FRANKLIN M. APPLE, Ph.G.

Any one conversant with various complaints that have been and are being made, by members of the medical profession, against

[1] Abstract of a paper read before the Philadelphia Branch of the American Pharmaceutical Association, March 5, 1907.

pharmacists who promiscuously renew prescriptions, will readily appreciate the need for the evolution of some plan whereby this practice can be controlled with evident fairness to all of the parties concerned.

From a careful study of my own prescription files I have come to the conclusion that an ever increasing number of medical men are desirous of limiting the use of their prescriptions to the patient for whom they are written, and, if possible, to the conditions existing at the time the patient was seen.

This tendency on the part of medical men is perhaps best illustrated by the ever increasing number and variety of requests not to refill prescriptions that are to be found, written or printed, on the files of the average pharmacy of to-day.

The printed requests particularly are increasing rapidly, and I may be permitted to cite you just a few of those that have come to my attention recently. They are as follows: "Not to be Renewed." "This prescription not to be refilled unless so ordered," "Note: This prescription is written for the party named above and for this time only. Do not refill without my written order." "Do not renew or copy." "Not to be renewed except upon orders in writing." "This prescription must not be renewed unless countersigned by physician giving it, and under renewed date!" "This prescription is intended for the present indications only, and is not to be renewed without the written consent of the physician."

Believing that any and all injunctions of this kind should be honored, so far as possible, it has been my custom to place upon all containers holding a compounded, restricted prescription the following sticker:—

Your physician directs that this prescription *is not to be renewed* without his consent.

In this connection I would like to call your attention to the first three words, they place the responsibility where it justly belongs and have a wonderful restraining influence over the patients, as many are afraid to have the prescription renewed knowing that their physicians deem it best not to do so.

To further eliminate the imperfections and the injustice to the honest pharmacists, of a bare statement "Not to be renewed," I have devised a plan that I believe to be equitable to all of the par-

ties concerned, viz.: the medical practitioner, the pharmacist, and the patient.

This plan is the use of a prescription blank that would be accepted as bona fide evidence of being a legal contract in that the patient could not disclaim a knowledge of the restrictive clauses of the injunction on the blank.

On the face of this prescription blank, immediately under the physician's name and address, is the following:—

NOTE.—The conditions under which this prescription is written will be found on the reverse side hereof.

On the reverse, and running across the centre of the prescription, is the following notice:—

This prescription is written for the party whose name appears thereon, for the present indications only; hence it is *not to be renewed* without my written consent, and *no copy of same is to be given.*

The pharmacist compounding it will kindly preserve same on his prescription file.

Date . . . . . Dr. . . . . .

The verbiage of the prescription is the weakest that I think prudent to use to meet the case. The medical man who chooses to use such a prescription blank can unquestionably control his prescriptions, but he at the same time assumes the responsibility to his patients for the restrictions; thereby putting him to an honest test if he wishes his prescriptions to be or not to be renewed.

I believe that the pharmacist receiving a prescription from a physician using this form of prescription blank, properly signed would have no alternative but to respect the request or order if he wishes to retain the good will and support of the prescriber.

The pharmacist is further relieved of any necessity of explaining the causes for the limitations placed on the prescription by the prescriber, and the inquiring patient should be referred directly to the author of the prescription for all necessary information.

The public should be protected against possible ignorance of the contents of compounded prescriptions, and the general adoption of a prescription blank of this type would effectually protect the patient from any and all possibilities of becoming unknowingly and unwittingly addicted to the habitual use of a prescription.

The merits of this plan are so manifest that it has been and is being used as the basis of the wonderfully satisfactory work done

by the Twenty-second District of New York City. It was offered to their medical men as an evidence of fair play in their propaganda for the more extended and general use of U.S.P. and N.F. preparations.

In conclusion I believe that there is sufficient demand for limiting the renewal of prescriptions, by medical men, to warrant the popularization of some satisfactory and efficient plan for doing so, and I also believe that the plan that I have just described to you is based upon justice, is safe legally, and where it has been tried honestly, has proven to be perfectly satisfactory.

CORRESPONDENCE.

STANDARDS IN PHARMACEUTICAL EDUCATION.

Editor of AMERICAN JOURNAL OF PHARMACY.

DEAR SIR:—I have read with much interest and profit your article in the March issue of the AMERICAN JOURNAL OF PHARMACY.

Permit me to call attention to a sentence on page 102, which reads as follows:

"And so if the youths of the country districts of Iowa, or Kansas, or Missouri have not, as is claimed by some, the opportunity for obtaining a high-school education, is that any reason why those in Ohio, or Michigan, or Pennsylvania should be excused for neglecting theirs?"

I should like to make the statement that Kansas is not willing to have herself classified with any geographical district where opportunities for a high-school education in rural districts are not obtained. There are already in Kansas one hundred and fifty accredited high schools; that is high schools accredited by the University of Kansas. There are seventy-five more high schools that give a two-year high-school course. The Barnes law, passed in 1905, grants public aid for high schools; this has already been made available in forty-three counties of the State, which will lead to the establishing of an estimated number of one hundred more four-year high schools.

Before the Barnes law went into effect, twenty-one counties of the State had already established county high schools. Thus sixty-four out of one hundred and five counties of the State offered free high-school tuition. It is estimated that within two years there will not

be a single county in the State that will not offer high-school privileges. There is no reason in the world why the educational standard should be kept low on account of high-school privileges in rural districts in Kansas.

I have noticed with regret the reflections which have been cast upon Kansas from the fact of her having been classified as above stated, and as a loyal Kansan I wish to enter my protest against any such reflections. We are endeavoring here to raise the standard of education as rapidly as possible, and if we should not do this we certainly should not offer the excuse of the lack of high-school privileges of the State.

L. E. SAYRE.

UNIVERSITY OF KANSAS, March 13, 1907.

AMERICAN MEDICAL ASSOCIATION.

REPORT OF THE COUNCIL ON PHARMACY AND CHEMISTRY.

We reprint herewith from *The Journal of the American Medical Association* an installment of the report of the Council on Pharmacy and Chemistry. A list of the new and non-official remedies tentatively approved by the Council was published in the February number of this JOURNAL (p. 67). The first installment of the descriptions of the remedies appeared in the March number (p. 112), and additional installments on some of them will appear from time to time. The importance of these reports is too evident to need comment. For the first time in the history of the organized profession, a scientific commission, whose ability and probity is above suspicion, has reported on preparations regarding which heretofore we have had only the report of those interested, financially and otherwise, in their exploitation.

ACETOZONE.

A mixture of equal parts of benzoylacetyl peroxide and an inert absorbent powder.

Actions and Uses.—Benzoylacetyl peroxide belongs to a class of compounds known as the organic peroxides in which an excess of oxygen has been combined in such a way that it is somewhat slowly given off in a nascent condition. On contact with water it hydrolyzes, forming benzo-peracid and aceto-peracid which exert marked

oxidizing and germicidal action. In consequence of this change, these compounds are thought to be particularly adapted for internal administration. The germicidal and antiseptic properties of this substance have been attested by the experimental results of several observers. It has been used in ophthalmic, aural and nasal practice with asserted good effects as an antiseptic. It has also been applied internally, especially in typhoid fever, with a view to the disinfection of the intestinal canal, and appears to be an intestinal antiseptic. Dosage.—Acetozone is generally employed in aqueous solution prepared as follows: Add acetozone to warm water in the proportion of 1 gramme to 1000 c.c. (15 grains to the quart), shake vigorously for five minutes, and allow to stand for about two hours. Decant the liquid as required. This solution may be drunk *ad libitum*, two quarts or more being taken by an adult in twenty-four hours. Acetozone is also used in oily solution as an inhalant. Manufactured by Parke, Davis & Co., Detroit, Mich.

ADNEPHRIN SOLUTION.

A sterile solution of 1–1000 of the suprarenal active principle in physiologic salt solution containing one half of 1 per cent. of metaform (chlorbutanol).

Actions and Uses.—The actions and uses of this preparation are described under Suprarenal Alkaloid. Dosage.—The dose internally is from 0·2 to 2·0 c.c. (3 to 30 minims) in water. Adnephrin is also used in oily solution as a spray, see Adnephrin Oil Spray, and in the form of ointment, see Adnephrin Emollient. Prepared by F. Stearns & Co., Detroit, Mich.

ADRENALIN.

The active alkaloid of suprarenal gland, prepared by the method of Takamine, see Suprarenal Alkaloid.

Dosage.—Locally, 1–1000 to 1–15000 solution, as the chloride. Internally, 0·3 to 2 c.c. (5 to 30 minims) of 1–1000 solution. Hypodermically, 1 to 15 drops of 1–1000 solution, diluted with sterile water. Manufactured by Parke, Davis & Co., Detroit, Mich.

ADRENALIN CHLORIDE SOLUTION.

Dosage.—See adrenalin. Prepared by Parke, Davis & Co., Detroit, Mich.

ADRENALIN SUPPOSITORIES.

One part of adrenalin to 1000 parts of oil of theobroma (cacao butter). Each suppository weighs about 1 gramme (15 grains). Prepared by Parke, Davis & Co., Detroit, Mich.

AGURIN.

Agurin—$C_7H_7N_4O_2Na + NaC_2H_3O_2$, a double salt of sodium acetate and theobromine-sodium.

Action and Uses—It acts like theobromine, over which it has the advantage of great solubility and that it is well tolerated by the stomach. While inferior in diuretic power to theophyllin (which see), it is said to have greater power in sustaining the diuresis produced. Dosage.—0·5 to 1 gramme (7 to 15 grains), preferably in wafers or capsules. If in solution, this should be freshly prepared (with peppermint water) and without sugar or mucilage. Manufactured by Farbenfabriken vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color and Chemical Company, New York).

ALPHOZONE.

Alphozone—$(COOH{\cdot}CH_2CH_3CO)_2O_2 = C_8H_{10}O_8$, an organic peroxide resulting from the action of hydrogen dioxide on succinic anhydride.

Actions and Uses.—Alphozone belongs to the class of organic peroxides, and by its powerful oxidizing power becomes a germicide and antiseptic. Dosage.—Alphozone is also marketed in the form of tablets containing each 0·065 gramme (1 grain) of alphozone, which are used for making solutions, 1 tablet to 60 c.c. (2 fluid ounces) of water giving a solution (1 to 1000) suitable for general external use; but, as a nasal douche, one tablet in 180 c.c. (6 fluid ounces) of water is often preferred. Manufactured by F. Stearns & Co., Detroit, Mich.

ALUMNOL.

The aluminum salt of β-naphtholdisulphonic acid, $Al_2(C_{10}H_5OH{\cdot}(SO_3)_2)_3 = Al_2C_{30}H_{18}O_{21}S_6$.

Actions and Uses.—It is an astringent and mild antiseptic. It is claimed that it can be used as a mild astringent, an irritant or a caustic, according to the strength of the solution, and it is asserted that it exerts a peculiar destructive action on gonococci. It has

been recommended for a variety of affections in which a caustic, astringent or antiseptic is indicated. It has been particularly recommended for gonorrhea in females, especially when affecting the endometrium. Dosage.—As a surgical antiseptic, in 0·5 to 3 per cent. solutions; in gynecology, in 2 to 5 per cent. solutions; in otology and laryngology, either as powder or in ¼ to 1 per cent. solution as douches, washes or gargles; as cautery, in 10 to 20 per cent. solution. Manufactured by Farbwerke, vorm. Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

ANTITHYROID PREPARATIONS.

Preparations obtained from the blood or milk of animals, after the removal of the thyroid glands. The use of these preparations is based on the theory that the thyroid gland secretes products which are toxic, but which neutralize, and are neutralized by, other toxic substances produced elsewhere in the body. Removal of the thyroid glands, therefore, leads to the accumulation of these second toxic substances as evidenced by the phenomena of cachexia strumipriva and myxedema. On the other hand, the blood or milk of such animals is capable of preventing the effects of a hypersecretion of thyroid substance, such as is supposed to occur in Basedow's disease (exophthalmic goiter). These views are still largely hypothetical; but the majority of clinical observers report markedly beneficial results in the milder forms of the disease and in obscure nervous disorders which are supposedly connected with thyroid hypersecretion. The effects are less pronounced in the more severe forms. The action is merely palliative and other methods of treatment should not be neglected. Improvement occurs in two or three weeks and is indicated by an amelioration of the nervous symptoms, tremors, palpitation, insomnia and excitability. The administration must be long continued. Oral and hypodermic administrations are equally effective, but the former is usually preferred. These preparations are not toxic, even when very large doses are used.

ARGENTAMIN.

An aqueous solution of silver nitrate and ethylenediamine, corresponding to 10 per cent. of silver nitrate.

Actions and Uses.—It is antiseptic and astringent like other silver salts, with the asserted advantage of being non-irritant and more

penetrating than silver nitrate. It is said to be useful in all cases where the non-caustic action of silver nitrate is indicated. Dosage. —It may be used in the anterior urethra in 0·25 to 1 per cent. solution; in the posterior urethra in from 1 to 4 per cent. solution; in ophthalmology in 5 per cent. solution. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin. (Schering & Glatz, New York.)

ARGONIN.

A soluble casein compound containing 4·28 per cent. of silver.

Actions and Uses.—Its actions and uses are similar to those of silver nitrate, but it is claimed to have greater power of permeating living colloid membrane than other silver albumoses. It is applied as an injection in 0·1 to 0·2 per cent. solution; in ophthalmic practice a 10 to 20 per cent. solution in glycerin may be used. Dosage. —It is generally used in 0·5 per cent. solution, but even 20 per cent. solutions have been injected without producing irritant symptoms. Manufactured by Farbewerke vorm. Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

ARGYROL.

A compound of a derived proteid and silver oxide, containing from 20 to 25 per cent. of silver.

Actions and Uses.—Solutions of argyrol (20 to 50 per cent.) are said to be non-irritating to mucous membranes. Taken internally it is said to be non-toxic. It is claimed to be an antiseptic. It is recommended in urethritis and cystitis, in conjunctivitis and in affections of the nose, throat and ear. Dosage.—It is employed in from 10 to 25 per cent. and even stronger solutions. Manufactured by Barnes & Hille, Philadelphia.

GLYCEROPHOSPHATES.

The salts of glycerophosphoric acid H_2 ($CH_2OH{\cdot}CHOH{\cdot}CH_2$) PO_4; usually the two remaining hydrogen atoms of phosphoric acid are replaced by the base; $Na_2(CH_2OH{\cdot}CHOH{\cdot}CH_2)PO$.

Actions and Uses.—These salts were introduced as "nerve foods" and tonics on the theory that their phosphorus, being a step nearer lecithin, is assimilated more readily than that of hypophosphites. Neither the experimental nor the clinical evidence is considered conclusive by all authorities. Dosage.—The potassium and sodium

salts may be given hypodermically 0·2 to 0·25 gramme (3 to 4 grains) in normal saline solution, or *per os* 0.25 to 0.65 gramme (4 to 10 grains) in water or syrup. The calcium, iron, lithium, magnesium and manganese salts 0·2 to 0·65 gramme (3 to 10 grains) doses, preferably in the form of tablets; the quinine salt in 0·1 to 0·33 gramme (1½ to 5 grains), and the strychnine salt in 0·001 to 0·003 gramme (1/60 to 1/20 grain) doses.

HEDONAL.

Hedonal, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH\ (CH_3)O \cdot CO \cdot NH_2 = C_6H_{13}O_2\ N$, a urethane differing from ethyl carbamate, U. S. P., in that the ethyl radicle has been replaced by the radicle of methylpropylcarbinol (pentan-2-ol.) $CH_3.CH_2.CH_2.CHOH.CH_3$.

Actions and Uses.—Hedonal appears to have a greater hypnotic effect than ethyl carbamate. It is said to be followed by no after-effects and is oxidized in the body to urea and carbon dioxide. It is recommended in insomnia due to mental overwork or nervous excitement occurring in the course of neurasthenia or hysteria. It is claimed to be particularly useful preliminary to anesthesia, a hypnotic dose being given and anesthesia effected with chloroform after the patient has been asleep for an hour. Dosage.—1 to 2 grammes (15 to 30 grains), administered dry, followed by a swallow of water, or in wafers or capsules. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Company, New York.)

HEXAMETHYLENAMINE METHYLENCITRATE.[1]

This substance, $C_6H_8O_7\ (CH_2)_6N_4 = C_{12}H_{20}O_7N_4$, is a compound of hexamethylenamine with anhydromethylencitric acid.

Actions and Uses.—It is a urinary antiseptic and germicide claimed to be more prompt and energetic in its action than hexamethylenamine, acting equally well whether the urine be alkaline or acid in reaction, rapidly clearing it up and allaying pain. Dosage.—0·6 to 1 gramme (10 to 15 grains).

HOLOCAINE HYDROCHLORIDE.

Holocaine hydrochloride. $CH_3 \cdot C\ (:N \cdot C_6H_4OC_2H_5)\ (\cdot NH \cdot C_6H_4 \cdot OC_2H_5) \cdot HCl = C_{18}H_{22}N_2O_2 \cdot HCl$, the hydrochloride of a basic con-

[1] This is the chemical name for a preparation on the market under the names of helmitol and urotropin, new.

densation product of paraphenetidin and acetparaphenetidin (phenacetin).

Actions and Uses.—It is a local anesthetic like cocaine, but having the advantage of quicker effect and an antiseptic action. Five minims of a 1 per cent. solution when instilled into the eye are usually sufficient to cause anesthesia in from 1 to 10 minutes. It is more toxic than cocaine and without effect on the pupil or blood-vessels. It is not so useful as cocaine when the vasoconstrictor effect of the latter is desired. It is said not to cause the scaliness of the cornea which sometimes results after the use of the older remedy. Dosage.—It is applied in a 1 per cent. aqueous solution. Manufactured by Farbwerke, vorm. Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

HYPNAL.

Hypnal, $C_{11}H_{12}N_2O \cdot CCl_3CH(OH)_2 = C_{13}H_{15}N_2O_3Cl_3$, antipyrine combined with one molecule of hydrated chloral.

Actions and Uses.—Hypnal is an analgesic and hypnotic resembling chloral in its action, but said to be less liable to produce injurious effects on the vaso-motor centre of the heart. It may be used where chloral is indicated, as in mild forms of mental excitement, incipient delirium tremens, and in insomnia caused by pain. Dosage.—1 to 2 grammes (15 to 30 grains); although supposed to be less toxic than chloral, larger doses up to 3 grammes (45 grains) should be used with caution. Manufactured by Farbwerke, vorm. Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

IODIPIN.

Iodipin is an iodine addition product of sesame oil containing 10 per cent. iodine, in organic combination.

Actions and Uses.—Iodipin acts in the system similar to the iodides, being broken up in a manner analogous to that described under bromipin, which see. Its action is more lasting and with less tendency to iodism. Manufactured by E. Merck, Darmstadt. (E. Merck & Co., New York).

EUMYDRIN.

Eumydrin $C_6H_5(HO \cdot CH_2)\ CH \cdot CO_2 \cdot C_7H_{11}N(CH_3)_2NO_3 = C_{18}H_{27}O_6N_2$, the nitrate of methylated atropine.

Actions and Uses.—Eumydrin is a mydriatic and antihydrotic, replacing atropine sulphate both internally and externally in corresponding doses. It is claimed that it dilates the pupil more rapidly than atropine and the dilatation is of shorter duration—being intermediate in these respects between atropine and homatropine. It is said to be much less toxic than atropine, so that larger doses may be given to secure the effect. It is particularly recommended for the treatment of night sweats, whooping cough and the relief of enuresis. Dosage.—Internally as an antihydrotic, 0·001 to 0·0025 gramme ($\frac{1}{60}$ to $\frac{1}{24}$ grain). Externally as mydriatic, in solutions about one-tenth stronger than the usual atropine solutions. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

EUPHORIN.

Euphorin, $CO(HN.C_6H_5)(OC_2H_5) = C_9H_{11}O_2N$, a compound closely allied to Æthylis Carbamas, U. S. P. (urethane) and differing from this by the replacement of the group NH_2 by NHC_6H_5.

Actions and Uses.—Euphorin is anodyne, antipyretic and antiseptic. It is recommended in rheumatism, sciatica, headache, etc. Externally it is recommended to be applied as a dusting powder in venereal and skin diseases, ulcers, burns, etc. Dosage.—0·5 to 1 gramme (8 to 15 grains) dissolved in wine or suspended in water; externally in powder, in lanolin ointment and in superfatted soap. Manufactured by Fabrik von Heyden, Radebeul near Dresden.

EUPHTHALMIN.

Euphthalmin, $C_{17}H_{25}NO_3.HCl$, a mandelic acid derivative of beta-eucaine.

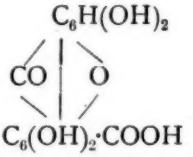
Actions and Uses.—Euphthalmin produces prompt mydriasis free from anesthetic action, pain, corneal irritation, or rise in arterial tension. It has little or no effect on accommodation, and this disappears more rapidly than with atropine, cocaine, hematropine, etc. In its effects on the general system, euphthalmin very closely resembles atropine. Dosage.—2 or 3 drops of a 5 to 10 per cent. solution, according to age of the patient and the nature of the case, are instilled into the eye. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin (Schering & Glatz, New York).

EUQUININE.

Euquinine, $C_2H_5O\cdot CO\cdot OC_{20}H_{25}N_2 = C_{25}H_{28}O_4N_2$, quinine ethyl carbonic acid ester.

Actions and Uses.—Euquinine is claimed to have the same action as quinine, with the advantage of being tasteless, owing to its insolubility in water and alkaline media. Dosage.—The same as quinine. Manufactured by Vereinigte Chininfabriken, Zimmer & Co., Frankfort a. M. (Merck & Co., New York).

GALLOGEN.

Gallogen.  $= C_{13}H_6O_8$, an

hydrous ellagic acid prepared from Divi-divi, the pods of *Cæsalpinia coriaria*, containing more than 50 per cent. of tannin.

Actions and Uses.—Gallogen is an astringent and antidiarrheic, slowly decomposed in the intestinal tract, thus exerting its astringent action gradually during its passage. It has been recommended in dysentery, cholera infantum, diarrhea, and is said to be useful even in those of a syphilitic or tuberculous origin. Dosage.—0·3 to 0·5 gramme (5 to 8 grains) for children; 0·6 to 1 gramme (10 to 15 grains) for adults, suspended in neutral or slightly acid media. Manufactured by Ad. Heinemann, Eberswalde (C. Bischoff & Co., New York).

THE AMERICAN PHARMACEUTICAL ASSOCIATION.

PHILADELPHIA BRANCH.

The ninth stated meeting of the Philadelphia Branch of the American Pharmaceutical Association was held on the evening of Tuesday, March 5, 1907, in the Hall of the College of Physicians.

The subject under discussion, "The Indiscriminate Renewal of Physicians' Prescriptions," elicited considerable difference of opinion, and the discussion itself was participated in by a rather unusual number of the members and visitors who were present.

The repeating of prescriptions, from a physician's point of view, was discussed by Dr. A. O. J. Kelly, who confessed that he, in

common with probably the greater majority of physicians, had no positive or well defined ideas on the limitations that should properly be set on the renewal of prescriptions.

On the one hand he believed that the renewal of prescriptions for many comparatively simple external applications, such as mild rubefacient liniments, and even the renewal of many prescriptions designed for internal use, such as stomachics and mild laxatives, could not well be objected to from any reasonable point of view.

On the other hand prescriptions containing potent remedies, or remedies that are at all known to create drug addiction or to do harm if long continued, should not be renewed indiscriminately, and should under no condition be trafficked in and never filled for any other than the original holder of the prescription.

In this connection Dr. Kelly quoted a number of instances that had come to his personal attention where the continued or the unwarranted use of potent remedies had done much, and in several instances at least permanent, injury.

Mr. Franklin M. Apple presented "An Efficient Plan for Controlling the Renewal of Prescriptions." Mr. Apple thought that the need for some well defined plan to prevent the renewal of prescriptions was well evidenced by the ever increasing number of physicians who were using some form of injunction on their prescription blanks. He discussed, at some length, the several forms of injunction that had been brought to his attention and compared these with the form that had been devised by him. This form he designated "The square deal prescription blank," as it puts the responsibility, for the refusal to renew a prescription, where it rightly belongs—on the physician.

Mr. Apple's prescription blank has on the face, immediately under the physician's name and address, the following:—

"NOTE—The conditions under which this prescription is written will be found on reverse side hereof."

On the reverse is the following:—

"This prescription is written for the party whose name appears thereon, for the present indications only; hence it is *not to be renewed* without my written consent, and *no copy of same is to be given.*

"The Pharmacist compounding it will kindly preserve same on his prescription file."

Mr. John K. Thum read a paper entitled "A Retrospect of Discussions on the Renewal of Prescriptions," in which he briefly reviewed a number of recorded discussions on this particular subject and quoted at length from an opinion by the late Dr. E. R. Squibb, expressed in Philadelphia in 1868. In discussing the desirability of having a law to regulate the renewal of prescriptions Dr. Squibb asserted that it would be unwise to introduce law or fixed rules to govern the renewal of all prescriptions and that after all it was but a matter of honesty, good sense and education on the part of the pharmacist.

Mr. Thum held that this opinion by Dr. Squibb covered the question fully as well to-day as it did forty years ago. He further expressed the belief that the pharmacist could and should control the indiscriminate renewal of prescriptions that are at all likely to do harm, by following the plan described by Mr. William Burke, of Detroit, at the semi-centennial meeting of the American Pharmaceutical Association, in Philadelphia, in 1902. Mr. Burke's plan was to discourage the refilling of prescriptions by attaching to all repeats a small sticker with a legend somewhat as follows:—

"More harm than good is often done by repeating these prescriptions, and it is well to consult your physician before refilling."

Dr. H. C. Wood, Jr., in opening the general discussion, said that we should never lose sight of the most important factors in this connection, and they are the protection of the public health and the guarding of patients against the ever possible generation of a drug habit.

He believed it to be wise for physicians to write the injunction not to renew the prescription on all orders for potent or habit-forming drugs, but he also believed that where this had been omitted it should be the duty of the pharmacist to guard the patient from the abuse of medicines of this kind. In concluding he expressed the opinion that common sense and forethought would tend to make the question of the renewal of prescriptions a very simple one.

The question was further discussed by Drs. Cattell, Robinson, Minehardt, Lowe, Thrush, Stewart, Smith and Kelly, and by Messrs. Remington, Gable, Blair, McIntyre, Wilbert, Greenawalt, Hunsberger, Apple and Thum. As noted before, the discussion elicited considerable difference of opinion on a number of the points that were involved, and at the conclusion of the discussion the secretary was

instructed to communicate with the proper officers of the Philadelphia County Medical Society with a view of having the members of that organization express their desires regarding the refilling of prescriptions.

Among the several questions that were brought up in connection with or bearing on the renewal of prescriptions it may be interesting to note the following, with a view of presenting them for further discussion :

Who owns the prescription ?

Is an agreement that does not bear the signatures of both parties valid ?

Would the Courts sustain a pharmacist in refusing to refill a prescription bearing an injunction " Not to be refilled "?

Should a pharmacist always retain the original prescription ?

Can a pharmacist, legally, refuse to give the patient a copy of the prescription ?

What is the status of the copy of a prescription ?

Should a reputable pharmacist fill or refill a " copy " ?

Granted that a " copy " should be recognized as a prescription, should the pharmacist differentiate between a copy written by a pharmacist and one written by the patient himself ?

What relation does the " copy " of a prescription bear to the printed prescriptions found in many of our daily papers ?

Should newspaper prescriptions be filled by reputable pharmacists ?

These questions, and many more that might be cited, presented themselves either directly or indirectly in the course of the discussion, and despite the fact that some of them at least would appear to be capable of a direct answer, they all allow of a difference of opinion, and together they amply justify the indecision of this particular meeting of the Philadelphia Branch.

This being the annual meeting, the discussion was preceded by a business meeting and election of officers.

The business meeting included the reports of several committees, the first of which, the committee on the death of Albert E. Ebert, reported the following preamble and resolutions:

WHEREAS, the death of Albert E. Ebert removes from the ranks of the American Pharmaceutical Association one of the most active workers and truest adherents, and constitutes an irreparable loss to the science of pharmacy in America. Now, therefore, be it

Resolved, That we, the members of the Philadelphia Branch of the American Pharmaceutical Association, in meeting assembled, record our sorrow at this loss. Be it further

Resolved, That we deplore his death as friends and as fellow workers in the field of pharmacy. Be it further

Resolved, That we heartily endorse the proposed monument to perpetuate the memory of Albert E. Ebert and urge that the members of the Philadelphia Branch of the American Pharmaceutical Association contribute toward the fund which is now being raised to erect a monument to his memory.

Dr. H. C. Wood, Jr., as chairman of the committee on exhibitions, made an exhaustive report, detailing what had been accomplished to date, and outlining, in a general way, the exhibition that it was proposed to make in connection with the annual meeting of the American Medical Association in Atlantic City during the coming summer.

Dr. Wood said, in part: "The authorities of the American Medical Association, through the Section on Pharmacology and Therapeutics, have given permission for an exhibit of pharmaceuticals to be held in connection with the regular scientific exhibit of the association, in which the Bureau of Chemistry of the Department of Agriculture has also promised to co-operate.

"Your committee desires in the first place to express its conviction that a most extraordinary opportunity is offered to this association, or branch, to render an inestimable service to the professions of pharmacy and medicine—a service which would inure not only to the benefit of humanity but also to the credit of the Philadelphia Branch of the American Pharmaceutical Association."

Dr. Wood then detailed the plans for this proposed exhibition and concluded with the statement that the committee "believe it much better not to exhibit too large a number of preparations, as a mass of material would likely lead to confusion, but to show a comparatively few types that would tend to have a permanent educational effect on the visiting medical men."

The election of officers for the coming year resulted in the selection of the following: President, Joseph P. Remington; First Vice-President, William McIntyre; Second Vice-President, William L. Cliffe; Secretary-Treasurer, Martin I. Wilbert.

M. I. WILBERT, *Secretary.*

DRUG AND FOOD INSPECTION DECISIONS.

NATIONAL FORMULARY APPENDIX.

The National Formulary is one of the standards recognized under the law. The question has been asked a number of times whether the appendix of this authority would be construed as part and parcel of the book itself. On page IV of the preface it is distinctly stated that the formulæ collected in the appendix of the National Formulary are "no longer designated as 'N. F.' preparations." This shows that these formulæ are not integral parts of the book under the law, which covers only those products of the National Formulary recognized as such by this authority. By this it is understood that if a drug product is sold under a name contained in the appendix of the National Formulary, it will not be necessary for such product either to conform to the standard indicated by the formula or to declare upon the label its own standard strength, quality, and purity if a different formula is employed in its manufacture. Such articles are, however, subject to the law in every other respect, as is the case of other medicinal products not recognized by the U. S. Pharmacopœia or National Formulary.

JAMES WILSON,
Secretary of Agriculture.

WASHINGTON, D. C., March 13, 1907.

DECLARATION OF THE QUANTITY OR PROPORTION OF ALCOHOL PRESENT IN DRUG PRODUCTS.

The question of stating the percentage of alcohol present in drug products has caused a multitude of inquiries. The following questions along this line serve as examples:

"Is it necessary to give the amount of alcohol present in U. S. Pharmacopœial or National Formulary products? It seems to me that such a requirement is absurd, and not contemplated within the spirit of the act. None of them are patent medicines. Will I be compelled to tell how much alcohol is present in such goods?"

"If we apply for and obtain a serial number, must we in addition to putting this number on our labels state the per cent. of alcohol?

"Will it be necessary to give the per cent. of alcohol present in such products as ether, chloroform, collodion, spirit of nitrous ether, and similar preparations?"

The law is specific on the subject of declaring the amount of alcohol present in medicinal agents, as can readily be seen from the following language: "An article shall also be deemed misbranded * * * if the package fail to bear a statement on the label of the quantity or proportion of any alcohol * * * contained therein." No medicinal preparations are exempt, whether they are made according to formulæ given in the U. S. Pharmacopœia or National Formulary or formulæ taken from any other source. The serial number, with or without the guarantee legend, does not exempt a preparation from this requirement. The law does not make any statement as to the amount of alcohol that may or may not be employed. It requires, however, that whatever amount be present shall be set forth on the label. The percentage of alcohol given on the label should be the percentage of absolute alcohol by volume contained in the finished product. The manner in which it should be printed is shown in F. I. D. 52.

JAMES WILSON,
Secretary of Agriculture.

WASHINGTON, D. C., March 13, 1907.

METHOD OF STATING QUANTITY OR PROPORTION OF PREPARATIONS (CONTAINING OPIUM, MORPHINE, ETC.) USED IN MANUFACTURING OTHER PREPARATIONS.

Many inquiries are received as to the method of stating the quantity or proportion of preparations (containing opium, morphine, etc.) used in the manufacture of other preparations. Of these the following are typical:

"If the label on the bottle were to bear the words 'Tincture of Opium,' I reason that as this is a definitive preparation, constituting a preparation of opium, and so definite as to its composition that to any intelligent persons it expresses definitely all that it is desirable to express, the use of this title alone should be sufficient. I feel that as a preparation it is distinct from opium, and if this particular tincture is used in the manufacture of a preparation the mention of it alone should be sufficient.

"Where extract or tincture of cannabis indica, or extract of opium, is employed in making other drug products, would it not be complying with the law if the use of such articles be clearly indicated on the label as prescribed by the law, or is it necessary to give the

actual amounts of the drugs themselves represented by these preparations ?"

Names of drug products bearing any of the names of the ingredients enumerated in the act are construed as representing "preparations" within the meaning of the act; and if the same are clearly declared upon the label as required by Regulations 17 and 30, it will not be necessary to give the actual amount of the primary drugs used or represented by such article. It is desirable, however, that the word or words used in the law shall constitute the first part of the name of the product. For example: "Opium, Tincture of"; "Cannabis Indica, Extract of," followed by the amount of tincture or extract used.

JAMES WILSON,
Secretary of Agriculture.

WASHINGTON, D. C., March 13, 1907.

RESOLUTIONS ADOPTED BY THE PHARMACEUTICAL PRESS OF AMERICA.

The following resolutions have been signed by the editors of the leading pharmaceutical journals of the United States:

WHEREAS, Albert Ethelbert Ebert died November 20, 1906; therefore, be it

Resolved, That we, the editors of the pharmaceutical periodicals of America, express our sorrow and testify to Mr. Ebert's long and exceptionally valuable life as that of one of the most able, indefatigable and conscientious of public-spirited pharmacists of this country.

Resolved, That Mr. Ebert, for some years editor of the *American Pharmacist*, always retained his interest in the pharmaceutical press and was ever ready to co-operate with the editors in a frank and liberal manner. Be it further

Resolved, That we heartily endorse the plan of erecting an Ebert memorial monument and will render the movement material assistance.

Resolved, That a copy of these resolutions be furnished the Committee on Memorial Volume of the American Pharmaceutical Association, and also be printed in our respective publications.

MARCH PHARMACEUTICAL MEETING.

The stated pharmaceutical meeting of the Philadelphia College of Pharmacy was held on March 19th, with William McIntyre in the chair.

A conjoint paper on "The Determination of Acetanilid and Phenacetin in Pharmaceutical Preparations," by Joseph L. Turner and Charles E. Vankerkleed, chemists of the H. K. Mulford Company, was read by the former. The authors presented two methods for the estimation of acetanilid and phenacetin in complex mixtures containing organic substances, and stated that such methods are made necessary by that provision of the Food and Drugs Act which requires an accurate statement on the label of the amount of acetanilid or phenacetin present in a preparation. (See page 151.)

C. M. Kline sent a communication from the research laboratories of the Smith, Kline & French Company, entitled "Some Notes on Opium from the Commercial Standpoint," which was read by W. A. Pearson, a member of the laboratory staff. The author described various commercial varieties of opium, and said that opium is produced in many countries in the East and differs largely in appearance, odor and strength according to the country or district in which it is produced, both on account of natural causes and differences in the method of handling. (See page 156.)

Dr. C. B. Lowe described the methods of incising the poppy capsule, and said that in order to prevent the admixture of opium with the tissues of the capsule considerable care is necessary in scraping off the opium. A question arising as to the number of seeds in the poppy capsule, Dr. Lowe said that it had been estimated that they average about 40,000.

Mr. Pearson said that last season in Michigan he had been successful in growing the opium poppy, both the white and red varieties, from seeds furnished by the U. S. Department of Agriculture. He, however, only collected about two drachms of opium, as a rain coming on soon after the incising of the capsules, washed away the product.

Attention was directed to a collection of commercial opiums which had been presented to the College some years ago by Messrs. Gilpin, Langdon & Co.

Referring to the U.S.P. assay method for opium, Mr. Pearson said

that he preferred the titration method to the gravimetric, as he had found the lime-water correction difficult. Mr. Turner, on the other hand, preferred the gravimetric method, and recommended the use of 4 c.c. of ammonia water. He also remarked that the same results could be obtained by the use of calcium hydroxide, which has the advantage of facilitating filtration.

Prof. Henry Kraemer gave a talk on "Some Recent Drug Adulterants and Substitutes." Attention was first directed to some specimens which had been presented by students of the college and others, as follows: Papaw fruits (*Carica Papaya*), by F. I. Lamas, of Sagua la Grande, Cuba; several thick quills of bark sold for cinnamon, by H. E. Strauss; a number of specimens of edelweiss (*Leontopodium*) collected in Switzerland, by E. M. Messmer; specimens of ginseng root and seed, and cotton, from Joseph Jacobs, of Atlanta, Ga.; some specimens of rye heads bearing ergot grains, by Eli Lilly, of Indianapolis. Professor Kraemer's observations on adulterated drugs will be embodied in a paper and published later.

FLORENCE YAPLE, *Secretary pro tem.*

NOTES AND NEWS.

GENEROUS DONATION TO THE FOOD AND DRUG LABORATORY FUND.—Benjamin T. and Samuel W. Fairchild, graduates of the Philadelphia College of Pharmacy, have shown their substantial interest in the progress of their Alma Mater by sending a check to Professor Remington for $500, to be applied to the building fund for the new food and drug laboratory. This donation is all the more acceptable because it is a free-will offering of two loyal sons.

JAPANESE LAC. The thesis presented to the faculty of the University of Bern for the degree of Doctor of Philosophy, by Professor Alviso B. Stevens of the University of Michigan, is a valuable monograph entailing considerable research work on the nature of the poisonous principle in Japanese lac (Kiurushi). The poisonous principle is intimately associated with the resin of the lac. It is obtained by adding 4 parts of alcohol to 8 volumes of a benzin solution of the lac, then thoroughly agitating the mixture and allowing it to stand. The lower alcoholic layer is of a reddish-brown color and contains the toxic principle. The author has been engaged for some time in a comparative study of the toxic principle of *Rhus toxicodendron* and *R. venenata* and that of the lacquer tree *R. venicifera*.

THE FOOD AND DRUGS ACT. Several pamphlets have been published containing a reprint of the National Food and Drugs Act in connection with the rules and regulations for its enforcement. One of the first of these pamphlets

to be published is that of the *American Druggist*, which contains a valuable article giving a legal opinion on "The Responsibilities of the Retailer" by William L. Perkins, Esq. Mahlon N. Kline, President of the Smith, Kline and French Company of Philadelphia, has also prepared a digest of the National Food and Drugs Act together with the regulations, which contains comments by Mr. Kline and others regarding their interpretation. The *National Druggist* has also published a pamphlet of 64 pages containing much valuable information. It is very fortunate that so much published material is available for the use of the trade in making clear the requirements of the new law and in showing associations and legislators the difficulties that must be avoided in framing state legislation.

PROF. A. B. STEVENS is the author of a book on "Arithmetic in Pharmacy" which was published some time ago by Merck & Co. The articles originally appeared in *Merck's Report* and the work is intended to cover all of the calculations required by the practical pharmacist. The book has been prepared not only for advanced students but for pharmacists and others who have been deprived of a liberal education. Pharmacists will find the book of considerable use and it will also be found helpful in the training of the apprentice.

THE EXTRA PHARMACOPŒIA of Martindale and Westcott has been brought up to date in the twelfth edition. One is surprised at the large amount of information which it contains that is the result of recent investigations. The pages on opsonins and the opsonic index, the preparation of the ferments of yeasts, the trypsin treatment of cancer, and the new drugs, chemicals, etc., are replete with useful information and make it one of the most desirable reference books in shop practice.

MERCK'S ANNUAL REPORT (1905) contains much interesting information on the advancements in pharmaceutical chemistry and therapeutics. The articles are most carefully prepared and contain much information that is not found either in the Progress of Pharmacy of the A. Ph. A. or in the pharmaceutical journals.

PROGRESS IN PHARMACY AND THERAPEUTICS. Lehn and Fink's "Notes on New Remedies" are always welcome. The present pamphlet, including abstracts from July, 1905, to July, 1906, contains much more than the title indicates, giving as it does a considerable number of analytical data, such as the test by Utz for differentiating Bombay and Banda mace, Milleau's method for detecting foreign fats and oils in cocoa butter, as well as other tests.

WOMEN'S ORGANIZATION OF THE N. A. R. D. This adjunct of the N. A. R. D. was established at the Boston meeting in 1905. Since that time branches have been formed in several of the larger cities, including Boston, Chicago, Washington, Atlanta, and Brooklyn. A local branch was organized in Philadelphia on February 15th. Mrs. Leslie O. Wallace of Boston, President of the National Women's Organization, was present and helped in the formation of the local chapter. The following officers were elected:—President, Mrs. William Estell Lee; first vice-president, Mrs. William T. Burk; second vice-president, Mrs. N. S. Steltzer; third vice-president, Mrs. W. H. Vandegrift; recording secre-

tary, Mrs. H. L. Stiles; corresponding secretary, Mrs. C. W. Shull; treasurer, Miss Emily Marsden.

The newly elected President appointed the following Board af Managers:—Mrs. T. H. Potts, Mrs. Charles Leedom; Mrs. C. L. Bonta, Mrs. Christian Moore, Mrs. J. C. Peacock, Mrs. J. Epstein and Mrs. Ida E. Stadelman. Four committees were appointed, with the following chairmen: Hospitality, Mrs. W. H. Gano; Social, Mrs. Charles Rehfuss; Educational, Miss Susanna G. Haydock; Press, Mrs. J. Leyden White.

Meetings will be held on the second Tuesday of each month at the College of Pharmacy. The society has 106 charter members.

THE COMMITTEE ON EXHIBITIONS of the Local Philadelphia Branch of the A.Ph.A. had a meeting to consider the exhibition in connection with the annual meeting of the American Medical Association at Atlantic City in June. It was decided to make the exhibition educational in character and to limit it to comparatively few preparations that could be used to displace some of the more objectionable of the proprietary nostrums now on the market. The subject will be further discussed at a coming meeting of the local branch when the details of the exhibit will be arranged.

PHILADELPHIA COLLEGE OF PHARMACY.

FOOD AND DRUG ANALYSIS COURSE.

A new course for the special instruction and training of Food and Drug Analysts, at the Philadelphia College of Pharmacy.

By reason of the passage of the National Food and Drugs Act on June 30, 1906, there has developed a pressing need for trained chemical and microscopical analysts, not only on the part of the United States Government, for the practical execution of this law, but also on the part of large manufacturing houses and dealers in drugs and chemicals.

The recent civil service examination of candidates to fill positions of analysts under the new act has demonstrated that the supply of such analysts is entirely inadequate to meet the present demands, and when the operation of the law begins to be felt the demand is certain to be greatly increased.

In addition to the National law, it is known that many States have similar legislation under consideration, if not already enacted. The present three years' course of this college leading to the degree of Doctor of Pharmacy covers much of the ground needed for the education of such analysts, and this is especially true of the regular third-year work, taken in connection with the Supplementary Spring Course. This latter course has been in operation for several years past and will be found to contain in the special chemical lectures on Food Analysis and Detection of Adulteration, together with the laboratory exercises connected therewith, and the practical course in the Microscopical Examinations of Foods and Drugs, much that bears directly on these subjects. However, the importance of the subject is such, in view of the sweeping legislation which has been enacted, that the trustees of the Philadelphia College

of Pharmacy have considered it necessary to provide greatly enlarged facilities, and to establish a distinct and independent two years' course to cover this work in a fuller and more complete way. They have, therefore, arranged to erect upon adjacent property (already owned by the college) a new laboratory, arranged and equipped for instruction in food and drug analysis, which laboratory it is proposed to have ready for use at the beginning of the regular session, October 1, 1907. (In the meantime the present laboratories will be used for the Summer Course, which will begin about May 20th.)

The regular course on this subject as planned by the Board of Trustees will cover two years of eight months each of *continuous* work, beginning in October of each year.

FIRST YEAR.

In the first year of this course, the students receive parts of the regular didactic chemical instruction given to the students of the first and second years of the regular three-year pharmacy course, as well as portions of the first-year and second-year pharmacy lectures of the same course. In addition to these, weekly exercises in the Botanical and Microscopical Laboratory on plant structure and microscopical technique will be provided, and in the Chemical Laboratory instruction will be given in *qualitative* chemical analysis, and the examination of unknown substances both liquid and solid, as well as a course upon the examination of the pharmacopœial chemicals for identity and purity.

SECOND YEAR.

In the second year the students will attend the complete course on general and pharmaceutical organic chemistry given in the third-year pharmacy course, as well as the supplementary course of lectures in food analysis and adulteration. A course in chemical mathematics is also arranged for the students of this year. In addition, a special course for students of this course only, will be given on the manufacturing processes and products of organic chemistry, as well as a course of lectures on the natural history and geographical distribution of foods and drugs, and a course upon the general medicinal properties of drugs.

All the time not required for these courses of lectures is given to the work of the microscopical and chemical laboratories. In the former, the microscopical study of powdered drugs, spices, foods, fibers, and vegetable products, together with fats and other animal products, is taken up in detail and a full course of technical microscopy is planned in this connection. These lectures and laboratory exercises will be supplemented by a number of excursions to manufacturing establishments and elsewhere.

In the chemical laboratory, the instruction in this year will cover the fundamental methods for gravimetric, volumetric, gasometric and colorimetric processes, and particularly in their application to pharmacopœial chemicals and preparations.

The different classes of food products will be taken up and the methods of analysis as prescribed in the "Provisional Methods of the Association of Official Agricultural Chemists," accepted as standards by the Department of Agriculture, will be gone over in detail with numerous examples for practice.

The study of preservative and coloring matters needed in order to detect

adulteration and sophistication of food products will also be carried out in fullest degree.

During this second year it is proposed to have in addition a special course of lectures to be given at frequent intervals by experts in different lines covered by the course of instruction, who will constitute a corps of special lecturers chosen because of their acknowledged position and authority in different lines of work. A great variety of important special topics can thus be presented that would be impossible to have in the ordinary lectures and laboratory exercises. It is the intention to cover in this course various lines of manufacturing chemistry as related to food products, and the commerce of staple articles, including the importation and exportation of crude and manufactured products.

QUALIFICATIONS FOR ENTRANCE.

Candidates for this course of instruction will be expected to satisfy the Dean of the Course of their possessing such an amount of previous scholastic education or practical training as to enable them to take up the work of the first year as given.

Those completing the first-year course and graduates of the Philadelphia College of Pharmacy, and other institutions having either a complete course leading to the pharmaceutical degree, or a scientific course leading to the same, will be admitted to the second year of this course in food and drug analysis, on presentation of their diplomas and transcript of their college record and approval of the same by the Dean.

SUMMER PREPARATORY COURSE.

Recognizing the urgency of the present demand for skilled analysts, and in answer to the expressed desire of many graduates of pharmacy schools to prepare themselves for this work, the trustees have arranged for a summer preparatory course for the spring and summer of 1907, to begin May 20th, and continue until the latter part of September. This is intended to afford graduates and others of mature years and practical experience the opportunity of preparing themselves by a rapid review of the work indicated as belonging to the first year of this course, to enter in the fall of 1907 upon the regular second year of this course.

For all but the most recent graduates this review of the chemical, pharmaceutical, botanical and microscopical work above enumerated is practically indispensable for the successful prosecution of the detailed work of the second year.

FEES.

The complete fee for each of the two years of this course, covering all lectures and laboratory instruction, shall be $150.

The fee for the summer preparatory course shall be $100. The usual matriculation fee of $5 is required of all students in the Philadelphia College of Pharmacy, whether in regular or special courses. This is paid but once, on the entrance of the student to any instruction in the College.